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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, DC 20005-3315

EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,502	GLOMBIK ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11,13,14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9,11,13,14 and 16* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment file December 02, 2003 has been received entered into the record and carefully considered. The following information provided in the amendment affects the application:

1. Claims 6-8 have been amended.

2. Claims 10, 12, 15 and 17 have been cancelled.

3. Remarks drawn to claim objection and rejection under 35 USC 112 second paragraph.

Applicants have requested the rejoinder of claims 9, 11, 13, 14 and 16 since these method claims are drawn to methods of using the compounds of claim 1 which has been found to be allowable. Claims 9, 11, 13, 14 and 16 have been rejoined.

Claims 1-9, 11, 13, 14 and 16 are pending.

Claim Objections

The objection of claim 8 has been overcome by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

A written description analysis involves three principle factors:

(1) field of the invention

(2) breath of the claims, and

(3) possession of the claimed invention at the time of filing for each claimed species/genus.

The Federal Circuit court stated that written description of an invention "requires a precise definition, such as by structure, formula, or chemical name, of the claimed subject matter sufficient to distinguish it from other material". University of California v. Eli Lilly and Co., 43 USPQ2d 1398 (Fed Cir. 1997). The court also stated "Naming a type of material generally known to exist, in the absence as to what the material consists of is not a definition of that material". Further, the court stated that to adequately describe a claimed genus, adequate must describe a representative number of species of the claimed genus, and that one skilled in the art should be able to "visualize or recognize the identity of the members of the genus".

Field of the invention

The present invention is drawn to diphenylazetidinones of formula I, composition of compounds of formula I with pharmacologically active agents and method of treatment of impaired lipid metabolism, hyperlipidemia, controlling serum cholesterol, treating insulin resistance and arteriosclerotic manifestations using compounds of formula I.

Scope and Content of the Claims

Claims 1-3 and 5 are drawn to compounds of formula I wherein at least one of R_1-R_6 is a (C_0-C_{30})-alkylene-(LAG) wherein LAG is an amino acid residue or an oligopeptide residue comprising 2 to 9 amino acids and composition comprising these compounds and a pharmaceutically acceptable carrier. The scope of the claim is seen to include any natural or synthetic amino acid or oligopeptide residue comprising 2 to 9 amino acids. Applicant claims a genus, which is generally known to exist in this art. Even though the disclosure recites some amino acid residues it is silent with regard to that which makes up and identifies the claimed genus, namely any synthetic or natural amino acid or oligopeptide residue comprising 2 to 9 amino acids, which is seen to be lacking a clear definition.

Possession of the claimed invention at the time of filing for each claimed species/genus

Examples 1-37 provided in the instant specification are drawn to synthesis of diphenylazetidinones that have an alkylene-sugar, alkylene-trialkylammonium and alkylene-O-(SO_2)-OH residues. There are no synthetic examples wherein an amino acid or an oligopeptide representative of the genus is linked via an alkylene to the diphenylazetidinones. A skilled artisan would not be able to envision the genus from just the these examples provided since the genus amino acid residue or oligopeptide residue comprising 2 to 9 amino acids is highly variable and does not have a core structure and function as the species. Hence, applicants do not have possession of the invention as instantly claimed.

Claims 9, 11, 13, 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating impaired lipid metabolism, hyperlipidemia, controlling serum cholesterol, treating insulin resistance and arteriosclerotic manifestations comprising administering to the host a therapeutically effective amount of a compound of the invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of one of ordinary skill
(D) The level of predictability in the art
(E) The amount of direction provided by the inventor
(F) The existence of working examples
(G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claims 9, 11, 13, 14 and 16 are drawn to methods for treating impaired lipid metabolism, hyperlipidemia, controlling serum cholesterol, treating insulin resistance and arteriosclerotic manifestations comprising administering to the host a therapeutically effective amount of a compound of claim 1. The claims are seen to be drawn to methods wherein there is an increase or decrease in the level of the said condition.

The state of the prior art

The examiner notes that prior art (WO 99/03861 and US 6525083) mention heterocyclic compounds for the reduction of insulin secretion, insulin resistance and hyperlipidemia. WO 99/03861 mentions that the compounds may be useful for treating insulin resistance. US 6525083 states that insulin resistance is not primarily due to a diminished number of insulin receptors but to a post insulin receptor binding defect that is not yet understood. In hyperlipidemia of type IIb and III there are modest elevations of LDL-cholesterol accompanied by more pronounced elevations of small dense LDL-cholesterol particles, VLDL and or IDL and total triglycerides (col. 1, lines 50-53 and column 2, lines 56-65). However, the prior art is silent regarding treatment methods for impaired lipid metabolism, hyperlipidemia, controlling serum cholesterol and treating insulin resistance.

The level of one of ordinary skill

The skilled artisan in this field is that of an MD for therapeutic administration and/or a Ph.D. skilled in the development of therapeutics.

The level of predictability in the art

Based on the disclosure of the prior art it is seen that the treatment of all of the said conditions is unpredictable.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to teach how to make and use the active agents instantly claimed for the treatment of impaired lipid metabolism, hyperlipidemia, controlling serum cholesterol and treating insulin resistance and arteriosclerotic

manifestations using the compounds instantly claimed. There are no correlative prior art procedures disclosed in the specification either.

The existence of working examples

The working examples set forth in the instant specification are drawn to experiments performed on rats. The examples provided show the cholesterol lowering effect in rats and an estimated human bioabsorption of a reference compound based on partition coefficient. However, there are no examples seen which show the effect of the instantly claimed compounds on conditions lipid metabolism, hyperlipidemia, controlling serum cholesterol other than lowering or for treating insulin resistance and arteriosclerotic manifestations commensurate in scope with the instant claims. There are no example of compounds wherein diphenylazetidinones comprising an alkylene-LAG wherein LAG is trialkylammonium, -O-(SO_2)-OH, amino acid or a an oligopeptide residue comprising 2 to 9 amino acids. A skilled artisan would not extrapolate the data provided in these two examples to the treatment of the said conditions, nor is there seen an art recognized correlation or guidance to accept such data as indicative of treating said conditions.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the treatment of impaired lipid metabolism, hyperlipidemia, controlling serum cholesterol and treating insulin resistance.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph of record, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been overcome by amendment

The rejection of claim 7 under 35 USC 112 second paragraph of record is being maintained. Claim 7 recites the term "affect". It is not clear what affect means. Affect is interpreted to mean both increase and decrease or to bring about a change other than an increase or decrease of lipid metabolism. The specification at page 8 recites the term "modulate" and also refers to antihyperlipidemic active compounds and antilipidemic active compounds. Both antihyperlipidemic and antilipidemic mean decreasing, whereas modulate encompasses increasing or decreasing to a certain proportion. Clarification is needed.

The following rejection for the rejoined claim is made of record.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites the term controlling. Since the term "controlling" encompasses both an increase and/or a decrease of cholesterol in claim 13, it is not clear what applicant intends said term to mean. It is also not clear what "need of control" means.

Conclusion

1. Claims 1-3, 5-9, 11, 13, 14 and 16 are rejected.

2. Claim 4 drawn to compounds of formula I wherein at least one of R_1-R_6 is a (C_0-C_{30})-alkylene-(LAG) wherein the alkylene group is substituted with an amino and carbonyl groups and wherein LAG is a sugar residue is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The compound of formula I wherein the structural limitation is at least one of R_1-R_6 is a (C_0-C_{30})-alkylene-(LAG) wherein the alkylene group is substituted with an amino and carbonyl groups and wherein LAG is a sugar residue is neither taught or fairly suggested by the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK